REMARKS

Claims 17-27 presently appear in this case. No claims have been allowed. The official action of July 24, 2007, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a process for upregulating T-cell activity in a mammalian subject by treating a population of T-cells ex vivo with a molecule that causes stimulation of glutamate receptor activation, using an amount of that molecule that is sufficient to stimulate glutamate receptor activation, thereby upregulating T-cell activity. That treated T-cell population is then administered to the subject. The molecule that causes stimulation of glutamate receptor activation is glutamate, a glutamate analog, an anti-glutamate receptor antibody, or an expressible polynucleotide encoding a glutamate receptor. The analog or the antibody is one that has a substantial degree of structural identity to glutamate and that stimulates glutamate receptor activation as measured by upregulation of T-cell cytokine secretion, adhesion, or chemotactic migration.

The present claims have now been amended so that they all now read on the elected invention of Group III and the elected embodiment of ex vivo treatment of the T-cells. Only claim 25 is directed to a non-elected species. However,

upon allowance of a generic claim, it is believed that this claim must then be rejoined and allowed.

Support for the claim language not previously appearing in the claims may be found in the present specification as follows. In claim 17, disclosure about use of an amount sufficient to stimulate glutamate receptor activation may be found, for example, at page 16, lines 7-12. Support for use of an anti-glutamate receptor antibody may also be found, for example, at page 16, lines 7-12, as well as at page 34, line 29, to page 35, line 15. The language about the analog or antibody being capable of stimulating glutamate receptor activation as measured by upregulation of T-cell cytokine secretion, adhesion, or chemotactic migration is supported, for example, at page 42, lines 12-25. See also page 28, line 29, to page 29, line 3, and page 32, lines 24-27. The language about an expressible polynucleotide is supported at page 16, lines 19-30, and page 39, line 29, to page 40, line 12.

As to claim 22, see page 16, lines 19-30.

As to claim 23, the language "neoplastic disease other than a T-cell cancer" is supported, for example, in the paragraph bridging page pages 40 and 41, insofar as treatment of neoplastic diseases in general by upregulation of T-cell function by glutamate is concerned. That T-cell cancers

should be excluded from the upregulating part of the present invention is apparent from the paragraph bridging pages 43 and 44, and particularly page 44, lines 5-9. Treatment of T-cell cancers, such as T-lymphoma, is the subject of the downregulation embodiment of the present invention. With respect to "an infectious disease or an infection," both of theses terms are present in the paragraph bridging pages 28 and 29, noting particularly line 24 and line 27.

As to claims 26 and 27, reference is made to the paragraph beginning at 33, line 9, particularly lines 14-17. It is believed that all of the other recitations of the claims appear in previously appearing claims.

In applicant's information disclosure statement of December 7, 2005, the examiner lined through reference WO99/50393 as it allegedly lacks a concise explanation of relevance. This refusal to consider WO99/50393 is respectfully traversed.

The examiner's attention is invited to MPEP 609.04(a)(III) relating to the requirement for a concise explanation of relevance for non-English language information. The second paragraph of this section includes the statement:

> Submission of an English language abstract of a reference may fulfill the requirement for a concise explanation.

The PCT publication at issue has an English language abstract. It is this abstract that serves as the concise explanation of relevance. See also the brief description of relevance that appears in the present specification at page 34, lines 1-19. Accordingly, the requirement of the rules in this regard was satisfied when that publication was submitted and, in any event, are now fully satisfied. Reconsideration of the examiner's refusal to consider this reference is therefore respectfully requested. Attached hereto is a new IDS form again listing this patent to facilitate the examiner's initialing at the appropriate place so that the reference will be made of record in this case.

Claims 5, 6, 8 and 9 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The examiner states that the language "modulating" a T-cell "activity" is not clear as to what direction, degree or type of modulation is required. Furthermore, the examiner states that it is not clear what activity is to be modulated or upregulated. This part of the rejection is respectfully traversed.

The term "modulating" no longer appears in the present claims. With respect to the term "activity," the new claims clarify that the T-cell activity being upregulated is an activity that one obtains upon stimulation of glutamate

receptor activation. As is apparent from the definitions of the glutamate analog and glutamate receptor, it is an activity that may be measured, *inter alia*, by upregulation of T-cell cytokine secretion, adhesion, or chemotactic migration. Accordingly, it is believed that this term, as used in the context of the present new claims, is no longer indefinite.

The examiner considers claims 5, 6 and 8 to be indefinite in the recitation of a "T cell activity modulating glutamate analog." The examiner suggests correction of hyphenation to correct this problem. This part of the rejection is respectfully traversed.

The term objected to by the examiner no longer appears in the present claims, thus obviating this part of the rejection.

Claims 5, 6, 8 and 9 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The examiner states that there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of glutamate "analogs." The examiner states that the instant specification on page 43 states that a "glutamate analog" refers to an amino acid, amino acid derivative or other molecule having a substantial degree of structural or functional identity to glutamate and therefore the claims encompass analogs that are

completely structurally unrelated to glutamate that have a similar functional identity. The examiner states that the specification only discloses related analogs that are structurally similar to glutamate.

The present claims have now been amended to specify that the glutamate analog is one that has a substantial degree of structural identity to glutamate and that stimulates glutamate receptor activation as measured by upregulation of T-cell cytokine secretion, adhesion, or chemotactic migration. This language is supported, for example, at page 42, lines 12-25. See also page 28, line 29, to page 29, line 3, and page 32, lines 24-27. Accordingly, the present claims are now specifically directed to that which the specification makes clear was in the possession of the applicant at the time that the present application was filed. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 5, 6, 8 and 9 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The examiner states that the specification provides insufficient evidence that the claimed method would function as a method for upregulating T-cell activity as broadly claimed. The examiner states that the language "a method of upregulating T-cell activity" encompasses upregulating a wide range of activities of

different types of T-cells. The examiner states that glutamate will decrease T-cell proliferation and, thus, while glutamate might be capable of upregulating certain T-cell activities the prior art teaches that glutamate does not increase all T-cell activities. This rejection is respectfully traversed.

The present claims do not require upregulation of every possible T-cell activity. As long as one T-cell activity is upregulated, the terms of the claim are met. Furthermore, the claim clarifies what T-cell activities are upregulated by indicating that it is the T-cell activities that one obtains upon stimulation of glutamate receptor activation. Those of ordinary skill in the art reading the present specification would be able to stimulate glutamate receptor activation and thereby obtain the T-cell activity upregulation described in the specification. Accordingly, reconsideration and withdrawal of this rejection, particularly with respect to the new language of the claims, are now believed to be in order and are hereby respectfully requested.

Claims 5, 6, 8 and 9 have been rejected under 35 U.S.C. 102(b), as being anticipated by Lombardi. The examiner states that Lombardi teaches a method of upregulating peripheral blood lymphocyte calcium signaling, which is a T-cell activity, by culturing lymphocytes with glutamate or

glutamate analog. The examiner states that this reads on exposure to or administration of glutamate to T-cells as recited in the instant claims. This rejection is respectfully traversed.

The present claims have now been amended to read only on the elected embodiment of *ex vivo* treatment of the T-cells and then administration of the treated T-cell population to the patient. Lombardi may teach contacting T-cells with glutamate, but there is no suggestion of administering the treated T-cells to a patient for any therapeutic purpose. Accordingly, Lombardi does not anticipate any of the present claims. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

Claims 5, 6, 8 and 9 have been rejected under 35 U.S.C. 102(b), as being anticipated by Frassanito as evidenced by Droge. The examiner states that Frassanito teaches a method of increasing cytokine production from T-cells from cancer patients by culturing the T-cells in RPMI medium. The examiner states that Droge evidences that RPMI contains glutamate and therefore Frassanito have exposed the T-cells to glutamate. Thus, the examiner considers that the reference clearly anticipates the invention. This rejection is respectfully traversed.

Regardless of whether RPMI 1640, as used by Frassanito, contains glutamate, Frassanito cannot anticipate the present claims as it does not include the step of administering the treated T-cell population to the subject. Accordingly, the present claims are not anticipated by Frassanito. Reconsideration and withdrawal of this rejection are respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /rlb/
Roger L. Browdy
Registration No. 25,618

RLB:jmd
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
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